UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,975	03/26/2004	Robert E. Davis	ACADIA.035A	7906

20995 7590 11/26/2008

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
11/26/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/809,975	DAVIS ET AL.	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-11 and 14-18* is/are pending in the application.

4a) Of the above claim(s) *14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/17/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 6-11, 14-18 are pending. Claims 14-18 are withdrawn from consideration. Claims 5, 11, 12 have been cancelled. Claims 1-4, 6-11 are being examined on the merits herein. The elected species is free of prior art. Hence the search was expanded to include other species in claim 6 and the following rejections have been made.

Response to Remarks

Applicants' arguments and the declarations regarding the rejection of Claims 1-4, 6-11 are rejected under 35 U.S.C. 112, first paragraph have been fully considered and found to be persuasive. Applicants' by way of declaration have shown that assays required to identify and select the compounds that are selective for the M(1) receptor can be done without undue experimentation. Hence the rejections are withdrawn. Applicants' arguments regarding the rejection of claims 1-4, 6-11 under 35 U.S.C. 103(a) as being unpatentable over Lavand'homme et al. (Anesthesiology, 1999, 91, 1455-61) Andersson et al. (WO 01/83472, publication date 8 Nov 2001) and further in view of Mitchell (J of Pain and Symptom Management, Vol. 21, 5, May 2001), rejection of claims 1-4, 6-11 under 35 U.S.C. 103(a) as being unpatentable over Lavand'homme et al. (Anesthesiology, 1999, 91, 1455-61) Andersson et al. (US 2002/0037886, publication date Mar 28 2002) and further in view of Mitchell (J of Pain and Symptom Management, Vol. 21, 5, May 2001) have been fully considered and found not to be persuasive. The rejections are maintained and are given below for Applicants' convenience. Accordingly, the action is made final.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lavand'homme et al. (Anesthesiology, 1999, 91, 1455-61) in view of Andersson et al. (WO 01/83472, publication date 8 Nov 2001) and further in view of Mitchell (J of Pain and Symptom Management, Vol. 21, 5, May 2001).

Lavand'homme et al. teaches cholinergic agents such as bethanechol, a muscarinic agonist reduces mechanical allodynia (tactile allodynia) after nerve injury to animals and may be useful in the treatment of neuropathic pain (see Abstract, p 1459, lines 4-6). The reference teaches the administration and determination of whether bethanechol reduced allodynia in the subject.

The reference does not teach the elected species, compounds in claim 6 to selectively activate the M (1) receptor subtype.

Andersson et al. teaches the compound of formula (VII) as in claim 6 of the instant application (p 13, line 7, claim 17, p 70, line 8, abstract, p 1, lines 4-10) as muscarinic M1 and M4 subtype. The reference further teaches the compound in a method of treatment of pain (p 4, line 26, p8, line 2, claim 57, p 78).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer a compound of formula (VII) for the treatment of neuropathic pain. The motivation to do so is taught by Lavand'homme et al. Lavand'homme et al teaches bethanechol, a muscarinic agonist to be useful in the treatment of allodynia and in the treatment of neuropathic pain. One of ordinary skill in the art would have been motivated at the time of the invention to use a compound of formula (VII) in the treatment of neuropathic pain as this compound has been shown to be a muscarinic agonist by Andersson et al. and one can expect similar success or superior results in relieving neuropathic pain by using this compound instead of bethanechol.

Lavand'homme et al and Andersson et al. do not teach a method of treating a subject for hyperalgesia, or thermal hyperalgesia and also do not teach the neuropathic pain to be associated with one of the diseases listed in claim 4.

Mitchell teaches that allodynia and hyperalgesia are clinical components of neuropathic pain and neuropathic pain conditions include cancer, painful diabetic neuropathy etc. (p 443, col. 2, lines 1-3, p446, col. 1, lines 7-11).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat subjects with hyperalgesia with a muscarinic agonist compound such as listed in claim 6 (formula VII). The motivation to do so is because Lavand'homme et al teaches that muscarinic agonist is useful in the treatment of allodynia a clinical symptom of neuropathic pain. It would have been obvious to one of ordinary skill in the art at the time of the invention to use a muscarinic agonist as listed in claim 6 to treat hyperalgesia which is another clinical symptom of neuropathic pain. Also, it would have been obvious to one of ordinary skill in the art to treat painful conditions associated with cancer, diabetes etc as Mitchell teaches them as neuropathic pain conditions and Lavand'homme et al teaches the usefulness of muscarinic agonist in the treatment of neuropathic pain.

Claims 1-4, 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lavand'homme et al. (Anesthesiology, 1999, 91, 1455-61) in view of Andersson et al. (US 2002/0037886, publication date Mar 28 2002) and further in view of Mitchell (J of Pain and Symptom Management, Vol. 21, 5, May 2001).

Lavand'homme et al. teaches cholinergic agents such as bethanechol, a muscarinic agonist reduces mechanical allodynia (tactile allodynia) after nerve injury to animals and may be useful in the treatment of neuropathic pain (see Abstract, p 1459, lines 4-6). The reference teaches the administration and determination of whether bethanechol reduced allodynia in the subject.

The reference does not teach the elected species, compounds in claim 6 to selectively activate the M (1) receptor subtype.

Andersson et al. teaches the compound of formula (VII) as in claim 6 of the instant application (para 234, example 93, claim 17) as muscarinic M1 and M4 subtype. The reference further teaches the compound in a method of treatment of pain (para 0028, 48, 303, claims 57, 72).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer a compound of formula (VII) for the treatment of neuropathic pain. The motivation to do so is taught by Lavand'homme et al. Lavand'homme et al teaches bethanechol, a muscarinic agonist to be useful in the treatment of allodynia and in the treatment of neuropathic pain. One of ordinary skill in the art would have been motivated at the time of the invention to use a compound of formula (VII) in the treatment of neuropathic pain as this compound has been shown to be a muscarinic agonist by Andersson et al. and one can expect similar success or superior results in relieving neuropathic pain by using this compound instead of bethanechol.

Lavand'homme et al and Andersson et al. do not teach a method of treating a subject for hyperalgesia, or thermal hyperalgesia and also do not teach the neuropathic pain to be associated with one of the diseases listed in claim 4.

Mitchell teaches that allodynia and hyperalgesia are clinical components of neuropathic pain and neuropathic pain conditions include cancer, painful diabetic neuropathy etc. (p 443, col. 2, lines 1-3, p446, col. 1, lines 7-11).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat subjects with hyperalgesia with a muscarinic agonist compound such as listed in claim 6 (formula VII). The motivation to do so is because Lavand'homme et

al teaches that muscarinic agonist is useful in the treatment of allodynia a clinical symptom of neuropathic pain. It would have been obvious to one of ordinary skill in the art at the time of the invention to use a muscarinic agonist as listed in claim 6 to treat hyperalgesia which is another clinical symptom of neuropathic pain. Also, it would have been obvious to one of ordinary skill in the art to treat painful conditions associated with cancer, diabetes etc as Mitchell teaches them as neuropathic pain conditions and Lavand'homme et al teaches the usefulness of muscarinic agonist in the treatment of neuropathic pain.

Response to Arguments

Applicants' arguments regarding the 103 rejections have been fully considered and found not to be persuasive. Applicants' argue that none of the cited prior art disclose compounds that have activity at muscarinic receptors used to treat neuropathic pain without alleviating acute pain. In response, Andersson et al. teaches the compound of formula (VII) as in claim 6 of the instant application as muscarinic M1 and M4 subtype. The reference further teaches the compound in a method of treatment of pain. The prior art teaches the same compound as claimed in the instant application for the treatment of pain. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art compound does not inherently possess the same properties as instantly claimed compound. The prior art teaches administration of the same compound claimed in the instant application in a method of

treating pain. Hence it inherently teaches the claimed method of treating neuropathic pain with out alleviating acute pain. Applicant has not provided any evidence of record to show that the prior art compound do not exhibit the same properties as instantly claimed. Any properties exhibited by or benefits provided by the compound are inherent and are not given patentable weight over the prior art. Applicants' further argue applicants' discovery of muscarinic agonists that alleviate neuropathic pain without alleviating acute pain is an unexpected result. In response as stated above, the prior art teaches administration of the same compound claimed in the instant application in a method of treating pain. Any properties exhibited by or benefits provided by the compound are inherent and are not given patentable weight over the prior art. Applicants' argue that they have discovered selective muscarinic agonists that differentiate between different types of pain and can alleviate neuropathic pain without alleviating acute pain and hence claims 1-4, 6-11 provide unexpected results and are not obvious. In response, Andersson et al. teaches the compound of formula (VII) as in claim 6 of the instant application (as muscarinic M1 and M4 subtype and further teach the compound in a method of treatment of pain. Hence just from Andersson's teachings alone it would have been obvious to one of ordinary skill in the art at the time of the invention that muscarinic agonist compounds of type I are effective in treating pain. Applicants' argue that one skilled in the art would not be motivated to use compounds of Andersson et al. for the indication taught by Lavand'homme. This is not persuasive because Lavand'homme et al. teaches that muscarinic agonists such as bethanechol, a muscarinic agonist reduces mechanical allodynia (tactile allodynia) after nerve injury to

animals and may be useful in the treatment of neuropathic pain. Hence a person of ordinary skill in the art would have been motivated to use a muscarinic agonist in a method of allodynia and in turn treating neuropathic pain in expectation of success and to provide similar or better therapeutic benefits.

Conclusion

No claims are allowed.

The rejections from the previous office action are maintained and accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617